

complexes comprising a therapeutic agent such as a peptide and a phosphorylated polymer. U.S. Application No. 09/184,413 filed November 2, 1998, teaches complexes comprising a therapeutic agent such as a peptide and a polymer bearing a non-polymerizable lactone. The teachings of the foregoing patents and applications are incorporated herein by reference.--

5. Please replace the Abstract of the Disclosure with the following:

--ABSTRACT

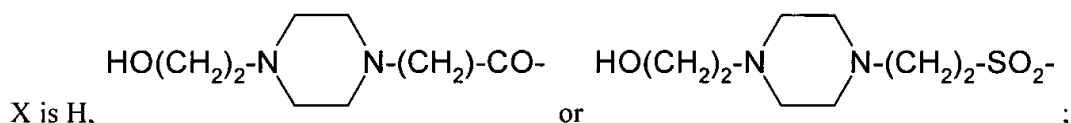
The present invention is directed to cyclic peptides of formula (I): $X-A^1\text{-cyclo(D-Cys-A}^3\text{-A}^4\text{-Lys-A}^6\text{-A}^7\text{)-A}^8\text{-Y}$, or a pharmaceutically acceptable salt thereof. The peptides bind selectively to the somatostatin subtype receptor type-5 and elicit an agonist effect from the somatostatin subtype receptors. The peptides are useful for treating a variety of diseases, including Cushings Syndrome, gonadotropinoma, hyperparathyroidism, Paget's disease, VIPoma, nesidioblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison Syndrome, hypersecretory diarrhea related to AIDS and other conditions, irritable bowel syndrome, pancreatitis, Crohn's Disease, systemic sclerosis, thyroid cancer, psoriasis, hypotension, panic attacks, sclerodoma, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Graves' Disease, polycystic ovary disease, upper gastrointestinal bleeding, pancreatic pseudocysts, pancreatic ascites, leukemia, meningioma, cancer cachexia, acromegaly, restenosis, hepatoma, lung cancer, melanoma, inhibiting the accelerated growth of a solid tumor, decreasing body weight, treating insulin resistance, Syndrome X, prolonging the survival of pancreatic cells, fibrosis, hyperlipidemia, hyperamylinemia, hyperprolactinemia and prolactinemia.--

COMPLETE LISTING OF ALL CLAIMS, WITH MARKINGS AND STATUS IDENTIFIERS
(Currently amended claims showing deletions by ~~strikethrough~~ and
additions by underlining)

1. (original) A peptide of the formula (I),

$$X-A^1\text{-cyclo(D-Cys-A}^3\text{-A}^4\text{-Lys-A}^6\text{-A}^7\text{)-A}^8\text{-Y,}$$
(I)

or a pharmaceutically acceptable salt thereof ,
wherein



A¹ and A³ are each independently the D- or L-isomer of an amino acid selected from the group consisting of Phe, Tyr, Tyr(I), Trp, 3-Pal, 4-Pal, Cpa and Nal;

A⁴ is L-Trp, D-Trp, L-β-methyl-Trp or D-β-methyl-Trp;

A⁶ is -NH-(CHR¹)_n-CO-, where n is 2, 3, or 4;

A⁷ is L- or D-Cys;

A⁸ is the D- or L-isomer of an amino acid selected from the group consisting of Phe, Tyr, Tyr(I), Trp, Nal, Cpa, Val, Leu, Ile, Ser and Thr;

Y is NR²R³ where R² and R³ are each independently H or (C₁-C₅)alkyl;

R¹ is selected from the group consisting H, (C₁-C₄)alkyl and -CH₂-aryl; wherein said aryl is an optionally substituted moiety selected from the group consisting of phenyl, 1-naphthyl, and 2-naphthyl, wherein said optionally substituted moiety is optionally substituted with one or more substituents each independently selected from the group consisting of (C₁₋₆)alkyl, (C₂₋₆)alkenyl, (C₂₋₆)alkynyl, aryl, aryl(C₁₋₆)alkyl, (C₁₋₆)alkoxy, -N(R⁴R⁵), -COOH, -CON(R⁴R⁵), halo, -OH, -CN, and -NO₂;

R^4 and R^5 each is, independently for each occurrence, H or (C_{1-3}) alkyl;

where the Cys of A^2 is bonded to the Cys of A^7 by a di-sulfide bond formed from the thiol groups of each Cys.

2. (original) A peptide according to claim 1 wherein

A^1 is L-Phe, D-Phe, L-Cpa or D-Cpa;

A^3 is L-Tyr, L-Trp or L-3-Pal;

A^4 is D-Trp;

A^6 is β -Ala or Gaba;

A^7 is L-Cys;

A^8 is L-Thr, L-Trp, L-Leu or L-Nal; and

R^2 and R^3 are each H;

or a pharmaceutically acceptable salt thereof.

3. (original) A peptide according to claim 2 wherein said peptide is of the formula

Cpa-cyclo(D-Cys-3-Pal-D-Trp-Lys-Gaba-Cys)-Nal-NH₂;

Cpa-cyclo(D-Cys-3-Pal-D-Trp-Lys- β -Ala-Cys)-Nal-NH₂;

Phe-cyclo(D-Cys-3-Pal-D-Trp-Lys-Gaba-Cys)-Nal-NH₂;

Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Gaba-Cys)-Nal-NH₂;

Phe-cyclo(D-Cys-Trp-D-Trp-Lys-Gaba-Cys)-Nal-NH₂;

Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Gaba-Cys)-Trp-NH₂;

D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Gaba-Cys)-Nal-NH₂;

D-Phe-cyclo(D-Cys-Tyr-D-Trp-Lys-Gaba-Cys)-Leu-NH₂; or

Phe-cyclo-(D-Cys-Tyr-D-Trp-Lys-Gaba-Cys)-Thr-NH₂;

or a pharmaceutically acceptable salt thereof.

4. (original) A peptide according to claim 3 wherein said peptide is of the formula

Cpa-cyclo(D-Cys-3-Pal-D-Trp-Lys-Gaba-Cys)-Nal-NH₂; or

Cpa-cyclo(D-Cys-3-Pal-D-Trp-Lys- β -Ala-Cys)-Nal-NH₂;

or a pharmaceutically acceptable salt thereof.

5. (original) A pharmaceutical composition useful for eliciting a somatostatin agonist response in a human or other animal which comprises an effective amount of a peptide of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof, and a pharmaceutically acceptable carrier.
6. (original) A method of eliciting a somatostatin agonist response in a human or other animal in need thereof, which comprises administering an effective amount of a peptide of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof to the human or other animal.
7. (original) A method of selectively binding a somatostatin subtype receptor type 5 in a human or other animal, which comprises administering an effective amount of a peptide of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof to the human or other animal.
8. (currently amended) A method of treating a disease or condition in a human or other animal in need thereof, which comprises administering a peptide of formula (I) according to Claim 1 or a pharmaceutically acceptable salt thereof to said human or other animal, wherein said disease or condition is selected from the group consisting of Cushings Syndrome, gonadotropinoma, hyperparathyroidism, Paget's disease, VIPoma, nesidioblastosis, hyperinsulinism, gastrinoma, Zollinger-Ellison Syndrome, hypersecretory diarrhea related to AIDS and other conditions, irritable bowel syndrome, pancreatitis, Crohn's Disease, systemic sclerosis, thyroid cancer, psoriasis, hypotension, panic attacks, sclerodoma, small bowel obstruction, gastroesophageal reflux, duodenogastric reflux, Graves' Disease, polycystic ovary disease, upper gastrointestinal bleeding, pancreatic pseudocysts, pancreatic

ascites, leukemia, meningioma, cancer cachexia, acromegaly, restenosis, hepatoma, lung cancer, melanoma, inhibiting the accelerated growth of a solid tumor, decreasing body weight, treating insulin resistance, Syndrome X, prolonging the survival of pancreatic cells, fibrosis, hyperlipidemia, hyperamylinemia, hyperprolactinemia and prolactinemia.

9. (original) A method of inhibiting the secretion of growth hormone, insulin, glucagon or pancreatic exocrine secretion in a human or other animal in need thereof, which comprises administering a peptide of formula (I) according to claim 1 or a pharmaceutically acceptable salt thereof to said human or other animal.
10. (original) A method of imaging cells containing somatostatin receptors *in vivo* in a human or other animal, which comprises administering a peptide of formula (I) according to claim 1, provided that at least one of A¹, A³ or A⁸ is Tyr(I), or a pharmaceutically acceptable salt thereof to said human or other animal.
11. (currently amended) A method of imaging cells containing somatostatin receptors *in vitro*, which comprises ~~administering~~ contacting the cells with a peptide of formula (I) according to claim 1, provided that at least one of A¹, A³ or A⁸ is Tyr(I), or a pharmaceutically acceptable salt thereof ~~to said human or other animal.~~